human Ig.

Gene and Genetic element, animal IT (for human Ig loci, transgenic nonprimate mammal transformation with)

is achieved by targeted disruption of the appropriate loci by

conjunction with breeding. Inactivation of the endogenous Ig loci

homologous recombination. Transgenic mice were prepd. that produced

```
ΪŢ
    .Immunoglobulins
        (genome for loci of, of human, transgenic nonprimate mammal
        transformation with)
     Molecular cloning
IT
        (of Ig genes, in prodn. of transgenic mice producing human Ig)
     Antibodies
IT
     Antiserums
        (of xenogeneic primate, prodn. of, by transgenic nonprimate
        mammal)
     Plasmid and Episome
IT
        (pmD.DELTA.J.Neo, as inactivation vector, prodn. of transgenic
        mice producing human Ig in relation to)
     Plasmid and Episome
IT
        (pmH.delta.J, as inactivation vector, prodn. of transgenic mice
        producing human Ig in relation to)
     Plasmid and Episome
IT
        (pmK.delta.J, as inactivation vector, prodn. of transgenic mice
        producing human Ig in relation to)
IT
     Mouse
        (transgenic, human Ig prodn. by)
IT
     Primate
        (xenogeneic antisera of, prodn. of, by transgenic nonprimate
        mammal)
     Gene and Genetic element, animal
IT
        (J, inactivation of, of mouse ES cells, in prodn. of transgenic
        mice producing human Iq)
IT
     Animal cell line
        (E14TG2a, mouse J genes inactivation in, prodn. of transgenic
        mice producing human Ig in relation to)
IT
     Antibodies
        (monoclonal, of xenogeneic primate, transgenic nonprimate mammal
        in prodn. of)
IT
     Mammal
        (nonprimate, transgenic, xenogeneic primate antisera prodn. by)
IT
        (stem cell, transformation of, of nonprimate mammal, with human
        Ig loci genome)
=> d bib ab it 113 1-3
     ANSWER 1 OF 3
COPYRIGHT (C) 1991 AMERICAN CHEMICAL SOCIETY
AN
     CA115(13):134000b
     Generation of xenogeneic primate antibodies by transformed
TI
     nonprimate mammal
     Kucherlapati, Raju; Jakobovits, Aya
AU
CS
     Cell Genesys, Inc.
\mathbf{L}\mathbf{0}
     USA
     PCT Int. Appl., 42 pp.
SO
     WO 9110741 A1 25 Jul 1991
PΙ
     W: AU, CA, JP, KR, NO RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
DS
     WO 91-US245 11 Jan 1991
AΙ
PRAI US 90-466008 12 Jan 1990
     US 90-610515 8 Nov 1990
IC
     ICM C12P021-06
     ICS C12N015-00
     15-3 (Immunochemistry)
SC.
SX
     3, 13
```

DT P .co PIXXD2 PΥ 1991 LA Eng Xenogenic primate antisera or antibody analogs are produced in a AB nonprimate mammalian host by immunizing the host with an immunogen. The transgenic host is substantially incapable of expressing endogenous Ig and is produced by repetitive transformations of embryonic stem cells by homologous recombination, preferably in conjunction with breeding. Inactivation of the endogenous Ig loci is achieved by targeted disruption of the appropriate loci by homologous recombination. Transgenic mice were prepd. that produced IT Gene and Genetic element, animal (for human Iq loci, transgenic nonprimate mammal transformation IT Immunoglobulins (genome for loci of, of human, transgenic nonprimate mammal transformation with) Molecular cloning IT (of Ig genes, in prodn. of transgenic mice producing human Ig) IT Antibodies Antiserums (of xenogeneic primate, prodn. of, by transgenic nonprimate mammal) IT Plasmid and Episome (pmD.DELTA.J.Neo, as inactivation vector, prodn. of transgenic mice producing human Ig in relation to) IT Plasmid and Episome (pmH.delta.J, as inactivation vector, prodn. of transgenic mice producing human Ig in relation to) IT Plasmid and Episome (pmK.delta.J, as inactivation vector, prodn. of transgenic mice producing human Ig in relation to) IT (transgenic, human Ig prodn. by) IT Primate (xenogeneic antisera of, prodn. of, by transgenic nonprimate mammal) IT Gene and Genetic element, animal (J, inactivation of, of mouse ES cells, in prodn. of transgenic mice producing human Ig) Animal cell line (E14TG2a, mouse J genes inactivation in, prodn. of transgenic mice producing human Ig in relation to) IT Antibodies (monoclonal, of xenogeneic primate, transgenic nonprimate mammal in prodn. of) IT

IT

IT

Mammal (nonprimate, transgenic, xenogeneic primate antisera prodn. by)

Embryo (stem cell, transformation of, of nonprimate mammal, with human Ig loci genome)

ANSWER 2 OF 3 COPYRIGHT (C) 1991 AMERICAN CHEMICAL SOCIETY

CA114(21):201177j AN Homologous recombination to inactivate MHC antigen genes and TI preparation of universal donor cells and chimeric mammalian hosts

```
. Kucherlapati, Raju S.; Koller, Beverly H.; Smithies, Oliver
ΑÚ
     Cell Genesys, Inc.
.CS
LO
     USA
     PCT Int. Appl., 39 pp.
SO
PΙ
     WO 9101140 A1 7 Feb 1991
DS
         AU, CA, JP, KR, NO
     RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE
     WO 90-US4178 25 Jul 1990
ΑI
PRAI US 89-385651 25 Jul 1989
     US 89-431872 6 Nov 1989
IC
     ICM A61K037-00
         C12Q001-68; C12N005-00; C07H015-12; A01H005-00; C12N015-00
SC
     3-5 (Biochemical Genetics)
SX
     15
DT
CO
     PIXXD2
PY
     1991
LA
     Eng
     Homologous recombination is employed to inactivate genes,
AB
     particularly genes assocd. with MHC antigens. Particularly, the
     .beta.2-microglobulin gene is inactivated for reducing or
     eliminating Class I MHC antigenes. The resulting cells may be used
     as universal donors. In addn., embryonic stem cells may be modified
     by homologous recombination for use in producing chimeric or
     transgenic mammalian hosts. Mouse embryonic stem cells were
     transformed with a .beta.2-microglobulin gene fragment contg. a
     neomycin phosphotransferase gene inserted into an exon.
     contq. inactivated .beta.2 microglobulin genes were microinjected
     into blastocysts, and the embryos were reimplanted into
     pseudopregnant female mice. After mating, gestation, and birth,
     baby mice heterozygous at the .beta.2-microglobulin gene were
                  Mating of male and female heterozygotes resulted in
     prodn. of mice homozygous for the mutant gene.
IT
     Wound healing
        (MHC antigen-deficient keratinocytes for, prodn. by homologous
        recombination of)
IT
     Mammal
     Mouse
        (MHC antigen-deficient, gene inactivation by homologous
        recombination in relation to)
     Transplant and Transplantation, animal
IT
        (cells for, MHC antigen-deficient, inactivation of MHC antigen
        genes by recombination for prepn. of)
     Animal cell
IT
        (mammalian, MHC antigen-deficient, prodn. by homologous
        recombination of)
IT
     Skin, composition
        (epidermis, cell, MHC antigen-deficient, prodn. by homologous
        recombination of)
IT
     Antigens
        (histocompatibility, class I, gene for, inactivation of,
        homologous recombination in, universal donor cells and transgenic
        mammal prodn. in relation to)
IT
     Antigens
        (histocompatibility, class II, gene for, inactivation of,
        homologous recombination in, universal donor cells and transgenic
        mammal prodn. in relation to)
IT
        (keratinocyte, MHC antigen-deficient, prodn. by homologous
```

recombination of)

```
Embryo
IT
        (stem cell, MHC antigen-deficient, prodn. by homologous
       recombination of)
    Microglobulins
IT
        (.beta.2-, gene for, inactivation of, homologous recombination
        in, universal donor cells and transgenic mammal prodn. in
       relation to)
     62213-36-9, Neomycin phosphotransferase
IT
        (gene for, .beta.2-microglobulin gene inactivated with, mammalian
       cells contg., prodn. by homologous recombination of)
IT
     59277-89-3, Acyclovir
                           82410-32-0, Gancyclovir
        (mammalian cells sensitive to, thymidine kinase gene insertion
        into MHC antigen gene by homologous recombination in relation to)
L13
    ANSWER 3 OF 3
COPYRIGHT (C) 1991 AMERICAN CHEMICAL SOCIETY
AN
    CA104(3):16020h
    Expression of N-myc in teratocarcinoma stem cells and mouse embryos
TI
    Jakobovits, Aya; Schwab, Manfred; Bishop, J. Michael; Martin, Gail
AU
    Sch. Med., Univ. California
CS
    San Francisco, CA 94143, USA
LO
    Nature (London), 318(6042), 188-91
SO
     3-3 (Biochemical Genetics)
SC
SX
    13, 14
DT
    J
CO
    NATUAS
IS
    0028-0836
PΥ
     1985
LA
    Eng
    Two mouse teratocarcinoma stem cell lines PSN-1 and F-9 expressed a
AB
     3.2-kilobase N-myc transcript. N-myc expression, equiv. to that
    found in PSN-1 cells, was also detected in poly (A) + cytoplasmic RNA
     from cells of an embryonic stem cell (ESC). Thus, 3 tumorigenic
    cell lines abundantly express N-myc. Southern blot anal. showed
    that PSA-1, ESC, and F9 cells appear to have the same no. of copies
    of the gene as do mouse neuroblastoma cells in which N-myc
                             Apparently, the abundant expression of
     expression is very low.
    N-myc is not the consequence of gene amplification. Further, N-myc
    is abundantly expressed in mouse embryos at mid-gestation (7.5-11.5
    day of development) and its expression appears to decrease as the
    embryo approached term. In adult mice, N-myc RNA was readily
    detected in poly(A) + RNA from brain, but was less abundannt in RNA
     from testis or kidney and not detected in spleen or liver.
IT
    Embryo
        (formation of, of mouse, gene N-myc expression during)
IT
    Mouse
        (gene N-myc expression in embryo and teratocarcinoma cells of)
    Development, mammalian
IT
    Brain, composition
        (gene N-myc expression in, of mouse)
IT
    Carcinoma
        (F9 terato-, gene N-myc expression in, of mouse)
ΙÜ
     Carcinoma
        (PSA-1 terato-, gene N-myc expression in, of mouse)
     Gene and Genetic element, animal
IT
        (N-myc, expression of, in mouse teratocarcinoma and embryo cells)
```

=> d bib ab it 114

```
L14 ANSWER 1 OF 2
COPYRIGHT (C) 1991 AMERICAN CHEMICAL SOCIETY
AN
     CA114(21):201177i
     Homologous recombination to inactivate MHC antigen genes and
ΤI
     preparation of universal donor cells and chimeric mammalian hosts
AU
     Kucherlapati, Raju S.; Koller, Beverly H.; Smithies, Oliver
CS
     Cell Genesys, Inc.
LO
     PCT Int. Appl., 39 pp.
SO
     WO 9101140 A1 7 Feb 1991
PΙ
         AU, CA, JP, KR, NO
DS
     RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE
ΑI
     WO 90-US4178 25 Jul 1990
PRAI US 89-385651 25 Jul 1989
     US 89-431872 6 Nov 1989
     ICM A61K037-00
IC
         C12Q001-68; C12N005-00; C07H015-12; A01H005-00; C12N015-00
SC
     3-5 (Biochemical Genetics)
SX
     15
DT
CO
     PIXXD2
PΥ
     1991
LA
     Homologous recombination is employed to inactivate genes,
AB
     particularly genes assocd. with MHC antigens. Particularly, the
     .beta.2-microglobulin gene is inactivated for reducing or
     eliminating Class I MHC antigenes. The resulting cells may be used
     as universal donors. In addn., embryonic stem cells may be modified
     by homologous recombination for use in producing chimeric or
     transgenic mammalian hosts. Mouse embryonic stem cells were
     transformed with a .beta.2-microglobulin gene fragment contg. a
     neomycin phosphotransferase gene inserted into an exon.
     contg. inactivated .beta.2 microglobulin genes were microinjected
     into blastocysts, and the embryos were reimplanted into
     pseudopregnant female mice. After mating, gestation, and birth,
     baby mice heterozygous at the .beta.2-microglobulin gene were
     identified. Mating of male and female heterozygotes resulted in
     prodn. of mice homozygous for the mutant gene.
IT
     Wound healing
        (MHC antigen-deficient keratinocytes for, prodn. by homologous
        recombination of)
IT
     Mammal
     Mouse
        (MHC antigen-deficient, gene inactivation by homologous
        recombination in relation to)
IT
     Transplant and Transplantation, animal
        (cells for, MHC antigen-deficient, inactivation of MHC antigen
        genes by recombination for prepn. of)
     Animal cell
IT
        (mammalian, MHC antigen-deficient, prodn. by homologous
        recombination of)
1T
     Skin, composition
        (epidermis, cell, MHC antigen-deficient, prodn. by homologous
        recombination of)
IT
     Antigens
```

(histocompatibility, class I, gene for, inactivation of,

mammal prodn. in relation to)

homologous recombination in, universal donor cells and transgenic

- IT Antigens
 (histocompatibility, class II, gene for, inactivation of, homologous recombination in, universal donor cells and transgenic mammal prodn. in relation to)
- IT Skin
 (keratinocyte, MHC antigen-deficient, prodn. by homologous recombination of)
- IT Embryo
 (stem cell, MHC antigen-deficient, prodn. by homologous recombination of)

=>

- IT Microglobulins
 (.beta.2-, gene for, inactivation of, homologous recombination in, universal donor cells and transgenic mammal prodn. in relation to)
- IT 62213-36-9, Neomycin phosphotransferase (gene for, .beta.2-microglobulin gene inactivated with, mammalian cells contg., prodn. by homologous recombination of)
- IT 59277-89-3, Acyclovir 82410-32-0, Gancyclovir (mammalian cells sensitive to, thymidine kinase gene insertion into MHC antigen gene by homologous recombination in relation to)